REMARKS

Claims 1, 3-7 and 93-120 were pending in the instant application. Applicants have cancelled claims 3-7, 105-106 and 108-109 without prejudice and reserve the right to pursue the subject matter of the cancelled claims in one or more related applications. Applicants have amended pending claim 1 and have added new claim 121 to more specifically point out and distinctly claim the invention. Support for the amendments and new claim may be found throughout the specification as filed, for example, support for the amendment to claim 1 and for new claim 121 may be found, *inter alia*, in paragraph [0004] at page 1, in paragraph [0006] at pages2-3, in paragraph [0016] at page 7, in paragraph [0035] at page 13-14, and in [0093] at pages 31-32.

After consultation with the Examiner, Applicants have also elected a new species of marker in connection with the invention of Group I as recited in the Restriction Requirement dated April 24, 2006. In particular, Applicants hereby elect as the species of marker the levels or amounts of β-APP, Aβ, and/or fragments thereof. In accordance with the instructions of the Examiner, Applicants have in this amendment withdrawn or canceled claims to the previously elected species of marker and "re-instated" those claims to the desired species of marker: previously pending claims 3-4, as drawn to species of cytokines, have been canceled, and the limitations of previously withdrawn claim 7, as drawn to β-APP or fragments thereof, have been included in claim 1 as amended herein. Accordingly, no new matter has been introduced. After entry of this amendment, claims 1, 93-104, 107, and 110-121 will be pending. Applicants submit that pending claims 1, 93-104, 107, and 110-121 read on the currently elected species.

Provisional Rejection For Obviousness-Type Double Patenting

The Examiner has maintained the provisional rejection under the judicially created doctrine of obviousness-type double patenting recited in the Aug. 8 Office Action. Without agreeing with the rejection, Applicants again request that the obvious-type double patenting rejection be held in abeyance until indication of allowable subject matter.

Objections to the Claims

The Examiner has objected to claim 108 for recitation of the term "agonize," wherein the

term is allegedly unclear. Applicants submit that, although not raised by the Examiner, a similar objection could have been raised against claim 105.

Applicants note that claims 105 and 108 have been canceled, rendering the instant rejection moot .

The rejections under 35 U.S.C. § 103 should be withdrawn

The rejection over Force in view of Tan

The Examiner has rejected claims 1, 93 and 110-120 under 35 U.S.C. § 103 as allegedly obvious over U.S. Patent Application Publication 2003/0059427 ("Force") in view of Tan et al., 2002, EMBO J 21:643-653 ("Tan 2002"). Applicants respectfully disagree with the Examiner's position for the following reasons.

Force is directed to the isolation of an anti-CD40R antibody and its characterization as a modulator of B cell activation, in particular, B cell proliferation. However, Force provides no motivation or suggestion that a compound of interest, *i.e.*, a modulation of CD40L-CD40R interaction, could be effectively evaluated in a system by determination of the level or amount of production of β-APP, or a fragment thereof, as instantly recited in claim 1. Thus Force does not render obvious the invention as instantly claimed.

Tan 2002 does not remedy the deficiencies of Force. Tan 2002 presents a study of the activity of CD40R in neuronal cells. Tan 2002 notes that ligation of CD40 in neural cells results in a cascade of events including upregulation of CD40 and stimulation of p44/42 MAPK activity, but does not teach or suggest that the CD40 pathway is involved in β-APP processing, much less that modulation of CD40L-CD40R interaction would result in a modulation of the level or amount of β-APP or a fragment thereof, *e.g.*, Aβ. Accordingly, Force, whether alone or in view of Tan 2002, fails to render obvious the invention as instantly claimed in claim 1. Because the instant combination fails to render obvious the invention of claim 1, it also does not render obvious the invention of claims 93-104, 107, and 110-121 as dependent thereon.

The rejection over Force taken with Tan(1999) in view of Gerritse and/or over Tan 1999 in view of Gerriste

The Examiner has rejected claims 1, 93, and 107-120 under 35 U.S.C. § 103 as allegedly obvious over Force taken with Tan et al., 1999, Science 286:2352-2355 ("Tan 1999"), in further view of Gerriste et al., 1996, P.N.A.S. USA 93:2499-2504 ("Gerritse"). The Examiner has also rejected claims 1, 3, 4, 93 and 107-120 under 35 U.S.C. § 103 as allegedly obvious over Tan

1999 in view of Gerritse. Applicants point out that claims 3, 4 and 108-109 have been canceled, rendering the instant rejections moot with respect to these claims. With respect to the pending claims, Applicants respectfully disagree with the Examiner's position for the following reasons.

As discussed above, Force fails to render obvious the invention of claim 1 as amended herein. Tan 1999 fails to remedy the deficiencies of Force. Tan 1999 teaches and describes the use of animal models and/or primary microglial cells derived from the animal models for evaluating compounds that affect CD40L/CD40R interaction. Tan is particularly directed to the characterization of systems wherein the indicator of ligand-receptor interaction is microglial cell activation. However, Tan 1999 offers no suggestion or motivation that a compound of interest could be effectively evaluated in a system wherein the indicator, *i.e.*, marker, of CD40R-CD40L modulation is the level or amount of β-APP or a fragment thereof. Thus, Tan 1999, alone or taken with Force, fails to render obvious the invention as instantly claimed.

Similarly, Gerritse fails to remedy the deficiencies of any of Force, Tan 1999, or Force in combination with Tan 1999. Gerriste is directed to the study of CD40R/CD40L interaction as a mediator of immune cell activation, in particular, in a model of experimental allergic encephalomyelitis ("EAE"). Gerritse describes the use of CD40 expressing monocytic cells in the model system, and concludes that the effects of compounds that modulate the CD40R/CD40L interaction were mediated via regulation of immune cell function, *e.g.*, immune cell activation. Thus, like Tan 1999, Gerritse cannot render obvious a screening system that is not based on the activation of an immune cell, *e.g.*, a system that is based on the production of β-APP or a fragment thereof as instantly claimed in claim 1. Accordingly, Gerritse, whether alone or in combination with Force and/or Tan 1999 fails to render obvious the instant invention as claimed in claim 1 or in claims 93-104, 107, and 110-121 as dependent thereon.

CONCLUSION

Applicant respectfully requests that the amendment and remarks made herein be entered and made of record in the instant application. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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